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EXCRETORY IRRITATION AS A FACTOR IN

CERTAIN SKIN AND OTHER ORGANIC INFLAMMATIONS

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APOLOGIA

In the year 1890, at the Birmingham meeting of the British Medical Association, the present writer read a short paper under the title of, "Dermatitis as an excretory symptom." The main object of that communication was to show the relationship of some forms of dermatitis to the excretory function of the skin. For ~~that~~ purpose a comparison was made of various rashes associated with internal conditions, such as the eruptions due to drugs, to exanthems, to gouty and other specific disorders. In these diverse phenomena there were certain common features, namely, an inflamed skin and a blood-supply containing a well defined

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irritant. Further inquiry showed that the irritant in almost every case affected the skin merely as one of a group of organs more or less actively engaged in excretion. In other words, the dermatitis was simply one of a general series of excretory irritations. This induction was drawn only after prolonged and careful consideration of the facts involved. Its further application has led to conclusions that in the present state of knowledge it seems impossible either to prove or to disprove. At the same time, if there be any truth in the theory of excretory irritation as a cause of some forms of skin inflammation it seems difficult to avoid the further proposition that a similar process may affect other excretory organs.

EXCRETION

In the following pages the term "Excretion" will be taken to mean the active state of an organ which results in throwing off certain normal and abnormal substances from the organism. By "normal substance" is meant any material usually ~~formed~~^{found} in the products of excretory glands, such as, water, salts, &c.: "abnormal" is applied to unusual or accidental materials, as for instance, ^{II}urea in milk, albumen in urine, mercury in sweat.

The modern view of the process is that the products of excretion are the result of the metabolic activity of the essential cell. This is well expressed by Dr. Lionel Beale as follows; ^{III}... "The characteristic substances present in the secretion are not merely separated from

^{III} Excretion. Dr. Lionel S. Beale. Lancet. p. 986, vol. j. 1896.

^{II} Urea in milk of women with kidney disease, mentioned by Wynter Blyth. Foods. 4th. Ed. Lond. 1896. Article. Milk Secreted by the Unhealthy

"the blood, but are actually formed by
"the so-called secreting cells."

Elsewhere he states that water is not passed on by the excreting cell as water, but is elaborated by the cell. That assumption may or may not be correct, but the specific micro-organisms of some infectious disease must pass through the excretory cells alive and presumably unaltered, if we are to judge from their continued infectivity. But if a living micro-organism be able to pass through the excretory cell unaltered it is difficult to see why a similar passage should not be open to urea, water, and other substances, especially when of an insoluble or non-irritating nature. At any rate we know that urate of soda and the pigments of jaundice may under some circumstances be visible upon the skin surface. Still, it seems likely that

few substances pass unaltered through the excretory epithelium, and that all, or nearly all, the characteristic materials of the various excretions are elaborated in the cells. It may be said, then, that everything that is excreted is formed from the blood by a vital process in the cell, and is then passed on or eliminated. Consequently, it follows that any substance taken up from the blood must become for the time being a factor in the metabolism of the cell, to which it may or may not act as an irritant.

INTERNAL IRRITANT

This term will be used in the present paper to signify any substance circulating in the blood which has the power of irritating the excreting cell, or, more generally, of setting up an inflammation

in any organ by which it may be eliminated from the body.

The main channels of exit of matters from the body are the lungs, the skin, the alimentary canal, and the kidneys. Each of those organs throws off water, carbonic acid, and nitrogenous products of more or less complex composition. In our present state of knowledge we may assume that their epithelial structures exert a selective action upon the materials brought to them by the blood. To a great extent the function of the various eliminating organs is interchangeable, so that they may act vicariously the one to the other. The exact channel of exit is to some extent determined physiologically by varying states of organic activity and selectiveness, by external conditions, and by the amount and the nature of the material to be excreted.

The foregoing statements are readily illustrated by the observations of everyday life and medical practice. By taking active exercise we throw the stress of elimination upon the skin and lungs. A compound colocynth pill excites copious excretion from the alimentary canal. Ample draughts of water or of broom tea increase the flow from the kidneys. Indeed, it is hardly too much to say that until recent years practical medicine was mainly based upon the interchangeable function of the excretory organs, which were relieved at each other's expense by the familiar processes of purging, sweating and diuresis. Even at the present time the control of the excretory functions may be regarded as the corner-stone of curative medicine.

But while the physician is thus able in many instances to determine the activity

of various excretory channels, it is often by no means clear how unaided nature avails herself of the interchangeability of excretory function. So far as the elimination of normal substances, (water, carbonic acid and nitrogenous matters), is concerned, the process by which the balance of excretion is maintained seems fairly intelligible. In the case of a labourer in a hay-field the maintenance of a standard body heat appears to be intimately connected with the result (through a complex nerve-vascular apparatus). The increased tissue heat and the high external temperature, acting directly and indirectly, charge the surface of the skin with blood; there is copious sweating, which reduces the body temperature by evaporation and to a certain extent lessens the kidney excretion. The amount

of material vicariously given off by the skin is represented by the difference between the scanty urine and the amount of urine that the labourer would have passed had he not been in the hayfield, but under ordinary conditions. If the same man took a Turkish bath he would lose about two pounds in weight, but that loss would only in part represent vicarious kidney elimination, as the actual amount of urine excreted during the bath would not be very materially reduced. These considerations show how carefully the subject of vicarious elimination must be approached in order to avoid fallacious deductions. On the other hand it should be noted that the flow from the kidneys is increased by the exposure of the skin to cold, while it is markedly lessened by free purging.

In the cases mentioned the determining influences of the shifted elimination are before us, but they are by no means so in the case of abnormal or accidental substances that have gained entrance to the system or have been elaborated therein. There is considerable irregularity, for instance, in the elimination of iodine or of the poison of gout. *This* may no doubt be partly explained by such factors as personal idiosyncrasy and the selectiveness, activity or incompetence of various organs. Quantity is another point that must be considered. A small amount of an accidental substance in the blood, e.g. iodine, is naturally eliminated by its usual organ of exit. When introduced in excess, however, one may easily imagine how it might overflow, as it were, into ~~the~~ other channels of exit. A few grains of sulphur

taken by the mouth would in the usual course be thrown off by the bowel or the kidneys; whereas a larger dose would escape in part by the lungs and skin. Nevertheless, in the majority of drug rashes the occurrence or the severity of the skin lesion appears to be little influenced by the amount of the irritant taken into the system. The state of the local blood-supply is probably another factor of importance in determining the excretory activity of any particular organ. The skin of an individual in the hot room of a Turkish bath is reddened and full of blood. In his case the distended cutaneous capillaries are brought into close relation with the glandular and Malpighian epithelium, so that for the time being the vascular arrangements of the skin closely resemble those of the kidneys. From this passing

glance it will be evident that the subject of the vicarious excretion of abnormal or accidental substances from the blood is full of doubts and difficulties. The writer's view is that the determination of the excretion of abnormal substances depends upon a variety of circumstances, in which idiosyncrasy, the functional activity, selectiveness and competency of organs, the nature and amount of the material to be excreted, and the conditions of environment all play essential parts.

IDIOSYNCRASY

It is not clear why one person should have a rash from an irritant, external or internal, while another, apparently under similar conditions, escapes any skin trouble. Nor can we

always account for an eruption clearing up in one individual, while it becomes chronic in another. A depressed state of health may of course predispose to invasion, and also delay the reaction of healthy tissues, whereby noxious material is got rid of by way of excretion, phagocytosis and so on. Such explanations, however, obviously do not cover the whole of the ground, and we can only say that there seem to be personal predisposing factors which we are unable to explain, and these we sum up under the convenient term "idiosyncrasy." Formerly, many authorities assumed a peculiarity of skin, which laid it especially open to attack, and which they called the "eczematous" or "dartrous" diathesis. That there is a difference in the resistance of individual epithelial structures seems more than likely. Thus, to most

folks a flea-bite is a mere trifling puncture, but in a few it gives rise to an acute circumscribed oedema as large as a shilling or a florin.

THE FUNCTION OF NORMAL EXCRETION

This subject need not be discussed here at any length. It is mainly effected by organs that excrete by virtue of epithelial structures variously arranged, but which all agree in having active epithelium cells on a basement membrane closely connected with the blood-supply.

THE EXTENT OF NORMAL EXCRETION

In the light of many clinical and pathological facts it seems likely that physiologists hardly recognise the full

nature and extent of the process of excretion. Any mucous membrane of the body, for instance, may take on an active excretory action in the presence of many of the substances circulating in the blood to which we have given the name of "internal irritants." Thus, the lining of the nasal cavity, under ordinary circumstances, is a simple mucus forming membrane, but when the blood is charged with iodine, it may by the excretion of that drug give rise to acute coryza. Or take the intestine of a person suffering from chronic nephritis; the accumulated urinary products in his system seek excretion by the bowel, and diarrhoea results, or they may in a similar way inflame the bronchi. In both instances a simple mucous membrane is for the time being converted into a vicarious excreting membrane. IV In the case of a gouty

IV Note. Dr. Jamieson says; "Eczema has its analogue in a no less important affection of internal organs, namely, in catarrh of the mucous membranes." Dis. of Skin. p.232.

person we may see every mucous membrane in the body thus attacked in turn, so that he may suffer from conjunctivitis, coryza, pharyngitis, laryngitis, bronchitis, dyspepsia, diarrhoea, cystitis, or urethritis, while his ordinary excretory organs are prone to severe recurrent and chronic inflammations.

Turning to drugs we may take the example of mercury absorbed through the skin and excreted by the salivary glands and bowel, with attendant salivation and purging.

A kind of vicarious excretion, moreover, appears to affect the serous and synovial cavities. That is to say, the internal irritants have the power not only of irritating the excretory outlets but also of inflaming the lining membranes of joints, bursae and serous cavities. Recently, the theory of excretory irritation advanced by the writer

has been applied by Mr. Sydney Stephenson to the iris, which most ophthalmic surgeons agree in regarding as the organ which secretes the aqueous humour. It will be noticed that the terms "secretion" and "excretion" are used here as practically synonymous. Whether the products of glandular activity are immediately thrown off from the body or not is simply an accident in their individual history. Moreover, from what has been already said, it seems certain that almost any of the so-called secreting membranes may become changed into excreting membranes. In the present paper, then, "excretion" will be used in a wide sense so as to include the less general term "secretion."

V The Excretory Origin of Certain Forms of Iritis
& Cyclitis. Sydney Stephenson. M.B. Lancet. Feb. 29. 1896.

SKIN DISEASES....CLASSIFICATION

Diseases of the skin may be divided, after Kaposi, ^{VI} into (1) Symptomatic, and (2) Idiopathic.

1. This division, the Idiopathic, includes lesions "produced by some agency affecting the skin directly," as scabies, heat, parasites, friction.

2. Symptomatic, described by Kaposi as;..."Those which are caused by the conditions of the blood and fluids in the organism itself or by the state of the general system; or are caused by disease of individual organs or systems; or come from hereditary conditions. Such diseases are the essential or incidental symptoms of these states and conditions.....symptomatic skin lesions."

Kaposi here recognises the causal connection between symptomatic skin

^{VI} Diseases of the Skin. Moriz Kaposi. English Edition. London. 1896. Ps. 61-2.

lesions and morbid conditions of other parts of the body, whether of blood or of organs; whether acquired or inherited. So far as one knows, however, he has not attempted to trace any actual bond between the skin symptoms on the one hand and the associated morbid conditions of blood and excretory organs on the other.

The following rough plan of etiology has been adopted by the writer to assist in the present inquiry.

A. Predisposing Causes. Sex, age, and other special conditions of the individual or his environment.

B. Determining Causes., which may be summed up in the one word "irritation." The nature of the irritant is often obscure, but it seems probable that the greater number of skin diseases may be traced ultimately to the action of irritants, which may be classified into

(1) external and (2) internal.

1. External Irritants; subdivided into (a) mechanical; (b) chemical; (c) mechanical and chemical combined.

(a) Mechanical...such as heat, which is the exciting cause of ~~the~~ rash induced by a Turkish bath, or by working in front of a furnace. Friction, as from clothing. Parasites, such as scabies or tinea circinata.

(b) Chemical, e.g., lime or sugar, (bricklayers' and sugarbakers' itch). Medicinal applications, for example, cantharides, mustard, croton oil, iodoform, tar. Soaps, especially the commoner sorts, in which there is an excess of free alkali.

(c) Mechanical and chemical irritants combined. Take the case of a scabies eruption, scratched by the patient into an eczema, raw and weeping,

and followed by suppuration. In this way a dermatitis started from purely local causes may be spread all over the body by means of the nails. This train of symptoms, it may be noted, would probably occur only in those persons who have what is sometimes called the "eczematous tendency." Under this heading may also be included micro-organisms and their products, which have attacked the epidermis, either as a primary invasion or as a secondary complication of a dermatitis due to some other cause.

2. Internal Irritants, which may be subdivided into (a) mechanical; (b) nervous; (c) chemical; ~~(d) chemical~~ and specific disease poisons.

(a) Mechanical, chiefly vascular, such as blood-stases due to varicose veins, or to the oedema of chronic

nephritis. *(This class does not fall within our definition of an "internal irritant"; neither does the next.)*

(b) Nervous In some cases skin lesions appear to be undoubtedly due to nerve influence, although that again may sometimes be referred to a remoter irritant, as, for instance, in herpes zoster following the administration of arsenic. On this account they may be provisionally included in this place, bearing in mind the possibility of pure neuroses of the skin, such as a local hyperidrosis of the palms. The nerve disturbances may be central or peripheral, (vaso-motor, trophic, &c.)

(c) Chemical and specific disease poisons. These include all substances circulating in the blood which are capable of setting up a dermatitis, and which fall under the definition of "internal irritants," already given. They may be discussed under the headings

of (A) Drugs. (B) Normal products in excess. (C) Specific disease poisons;

1st (a) due to micro-organisms; ~~2nd, chemical, this last being further subdivided~~

into (d) chemical poisons produced in the system -

the system, and (e) chemical poisons

produced by micro-organisms. *

The present inquiry is concerned with class "C" only, ~~of the internal irritants~~, and discusses skin or other organic lesions produced by drugs or specific poisons ^(other than drugs) circulating in the blood. Few people, whether dermatologists or general physicians, would dispute the proposition that a dermatitis is the invariable result of some causa irritans; the moot point is how the local irritation is brought about, and its exact relation to accompanying systemic morbid phenomena. To ascertain, or to attempt to ascertain, the common underlying factor between symptomatic skin

Note. A better classification of subdivision "C" would be into (1) Drugs, (2) Vital, the latter being further divided into (a) microorganisms (b) products of micro-organisms (c) chemical substances produced in the body. The classification ^{above} adopted, however, has some advantages in the present inquiry.

diseases and blood-borne irritants is
the primary object of the present thesis.

The three subdivisions of
(1) Drugs, (2) normal products in
excess, (3) specific disease poisons
to be now discussed are those
which have the power of producing
eruptions of the skin when intro-
duced into the blood, & which fall
under our definition of "internal
irritants". (page 5.)

Class C, Chemical & Specific Disease Poisons.

~~INTERNAL IRRITANTS.~~ A. 1. DRUGS.

The following, taken from Gould's Dictionary of Medicine, is a fairly full and accurate list of drugs that, ~~when~~ taken internally, have been known to cause eruptions of the skin. ^{VII} "Antifebrin produces a kind of cyanosis; antipyrin, an erythema that may be general or partial, but symmetric, affecting the extensor aspects in preference to the flexor, and the limbs more than the trunk; papules, vesicles, and bullae have been noted; arsenic produces an urticarial, erysipelatoid dermatitis of the face and eyelids, a papular rash on the face, neck and hands, herpes zoster, and in large doses pustular, ulcerative, or gangrenous eruptions; belladonna, a diffuse erythematous blush and a scarlatiniform eruption; boric acid, an

^{VII} "Dictionary of Medicine, Biology & Allied Sciences." George M. Gould. M.D. New York & London. 1896. Article "Dermatitis Medicamentosa."

"erythema; borax, psoriasis, eczema and
"erythema; bromin and bromids, pustular
"erythematous, urticarial, and squam#ous
"eruptions; cannabis indica, a vesicular
"eruption; chlorate of potash, a fiery
"erythematous and papular eruption, and
"cyanosis; chloroform, purpuric spots;
"chloral hydrate, erythema, scarlatiniform,
"bullous, erysipelatous eruptions;
"chloralamid, scarlatiniform; chrysarobin,
"erythema, vesicles; cod-liver-oil,
"vesicular eruption, acne; cubebs,
"papular erythema; digitalis, scarlatini-
"form, papular erythema; iodin and
"iodids, pustulae, vesicular or bullous,
"purpuric, erythematous, urticarial;
"iodoform, punctiform, papular and
"erythematous; mercury, erythematous,
"exfoliative dermatitis; morphin,
"erythematous; phosphoric acid, bullous,
"purpuric; quinine, eczema, erythematous,
"urticarial, purpuric, vesicular, bullous;

"resin, urticarial; rhubarb, hemorrhagic
"and pustular bullae; salicylic acid,
"erythema, urticaria, bullae, petechiae,
"vesicles, pustules; santonin, urticaria;
"stramonium, erythema; strychnin,
"scarlatiniform-pruritus, miliaria;
"sulphonal, erythema, purpura; tannin,
"urticaria; tar, erythema, vesicles and
"bullae, acne; terebene, papular
"erythema; tuberculin, scarlatiniform;
"turpentine, erythema, papules, vesicles."

We shall next consider in detail
points connected with a few of these
symptomatic drug rashes.

~~INTERNAL IRRITANTS CLASS A. DRUGS~~

ARSENIC,

Multiform rashes may follow the internal use of arsenic. These may be erythematous, urticarial, papular or pustular; there may be keratosis of the palms and soles, with pitting of skin; and herpes zoster appears to develop with undue frequency either during or after a course of arsenic. Another cutaneous symptom is deep brown pigmentation. On this point Unna quotes Wyss, ^{VIII} who states that the basal prickle layer of the epidermis was deeply pigmented in a choreic child treated with the drug. In his smaller Atlas of Clinical Surgery ^{IX} Mr. Jonathan Hutchinson has three interesting plates showing arsenic psoriasis, keratosis and cancer. The multiform and extensive nature of these lesions has

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- ^{VIII} *Histopathology of Diseases of the Skin*. Dr. P. J. Unna. English Translation. Norman Walker, M.D. Edinburgh. 1896. p. 974.
- ^{IX} *Smaller Atlas of Clinical Surgery*. Jonathan Hutchinson, F.R.S. Lond. 1895. Plates ^{XVIII}, ^{XIX}, ^{XX}.

X

been summed up by Dr. C. Rasch, quoted by Wood, ^{XI}as follows. "1. Pigmentation. "2. Erythematous and desquamative "eruptions. 3. Urticaria and subcutaneous oedema. 4. Vesicular eruptions. "5. Bullae. 6. Papules. 7. Pustules "and ulcers. 8. Purpura. 9. Shedding "of the hair and nails. 10. Keratosis."

The chief path of exit of arsenic from the system is by the kidneys, but it also escapes through the mucous membranes of the alimentary canal (e.g. after cutaneous absorption), through the skin, and even in the secretions of the lachrymal and salivary glands. Wood quotes a case reported by Dr. Pinkham (Boston Med. and Surg. Journl. 1878, p. 358.) in which the liver, kidneys, and epithelial lining of the peptic glands were almost destroyed.

XII

Salkowsky, of Moscow, showed that in rabbits poisoned by small doses of arsenic

XI Therapeutics. Prof. Wood, of Pennsylvania. 9th Edition, (English). 1894. p. 559.

X Ann. Dermat et Syph. Tome IV. Dr. C. Rasch. Wood. op. cit. p. 548

XII Virchow's Archiv. Bd. XXXIV p. 77. Dr. Salkowsky.

the liver was enlarged and fatty, with degeneration of the central cells of the acini. The renal tubules were choked with fat globules, and their epithelium destroyed.

From these statements it appears that arsenic is an internal irritant capable of inflaming the chief excretory organs (except perhaps the lungs), and that it is highly damaging to the epithelium. Lastly, it may be noted that externally arsenic acts as a powerful irritant and caustic.

MERCURY

The internal use of mercury may be followed by various forms of dermatitis varying from a mild fugitive erythema to papular and severe desquamative lesions.

The drug is eliminated by many channels of exit, a fact which holds good whether it is taken by the mouth or introduced into the system in other ways, as by inunction. ^{XIII} Wood, who gives a capital account of drug eliminations, observes. "Mercury has been found in the blood, "urine, the serum and pus of ulcers, "saliva, faeces, seminal fluid, the milk "of nursing women...indeed, in every conceivable secretion and tissue. Haller, "of Vienna, found it in the aborted "foetuses of salivated women, and Mayençon "and Bergeret in the urine of a baby whose "nurse was taking calomel; and both of "these observations have been confirmed "by Wellander." Mercury is capable of causing considerable damage to excretory organs, as proved by the diphtheritic colitis, the skin lesions, and the renal

^{XVII} Therapeutics. Wood. 9th Ed. 1894. p 566.

mischief found after death from poisoning by corrosive sublimate.

Mercury, then, acts as an irritant to all the excreting organs, with damage to their epithelium. It also often acts as an external irritant.

IODINE AND IODIDES

~~XIV~~

The internal use of iodine and its compounds may cause erythematous rashes about the arms, face, and neck; an eczematous state of the scalp; a pustular, acne-like rash; besides bullous tubercular eruptions. Mr. Hutchinson ^{XV} has two excellent coloured illustrations in his Smaller Atlas of a patient thus affected. The eruption consisted of scattered tuberos fungating masses, due to large doses of iodide of potassium. The patient died of exhaustion shortly after

^{XIV} Dictionary of Practical Medicine. Kingston Fowler M.D. Lond. 1890. Article "Medicinal Rashes." Dr. J. J. Pringle

^{XV} Smaller Atlas of Clinical Surgery. Mr. Jonathan Hutchinson. 1895. Plates III & IV.

the discontinuance of the drug. Iodine is usually eliminated by the kidney, but it may also escape by any of the mucous membranes or by the skin. Many observers have reported albuminuria during its administration, and have even asserted it to cause true tubular nephritis. In any case there can be no doubt that iodine exerts an irritant effect when excreted by the skin. Its direct escape from the latter organ has been maintained by Dr. P. W. Taylor (American Journl. of Syphilography and Dermatology, April, 1893.), and has also been reported by Adamkiewicz and Guttman, ^{XVI} quoted by Dr. Pye Smith. ^{XVII}

The group of symptoms known as "iodism," namely, dermatitis, coryza, and gastr/o-intestinal trouble follows when iodine is thrown off by channels other than the kidney. Any or all of these symptoms

^{XVII} Diseases of Skin. P. H. Pye-Smith. M.D.
London. 1893. p. 154.

^{XVI} Virchow's Archiv. 1878. vol. Lxxiv.; "Charité annalen, vol. iii", p. 381, 1878.

note. Dr. Pye-Smith (loc. cit.) says of iodide + bromide rashes, "In both cases there appears to be a true excretion of the drug through the sebaceous glands."

may ensue when the iodine is introduced into the system otherwise than by the mouth, as by painting the skin, or by injection into an ovarian cyst. Some writers assert that iodism is more apt to occur when kidney action is defective. Thus, Dr. Pringle ^{XVII} says;..."Renal disease "and cardiac weakness strongly predis- "pose to the occurrence of bromide and "iodide rashes owing to the deficient "elimination of the drugs in the presence "of such conditions." Dr. Radcliffe Crocker ^{XIX} remarks;..."Iodide eruptions, "especially the severer forms, are very "liable to occur when there is any renal "inadequacy, whether that is due to dis- "ease of the kidney itself, or to a "weakly acting heart....Iodide of potassium "is a powerful diuretic and as long as "diuresis is kept up there is often no

^{XVII} Fowler's Dictionary of Medicine. p. 505.

^{XIX} Diseases of the Skin. Radcliffe Crocker, M. D.
2nd Ed. Lond. P. 304.

"eruption, but when the drug is stopped
"for a few days the diuresis stops, and
"the iodine, not being removed fast
"enough, excites an eruption." A simple
explanation of the renal inadequacy would
be found if we assume the iodine to
irritate the excreting epithelium of the
kidney, as it certainly does that of the
skin and mucous membranes. The dis-
turbance to the kidney would hinder its
function, so that the stress of subsequent
elimination of the irritating iodine
would be thrown upon other excretory
organs.

Iodine, then, is excreted chiefly
by the kidneys. It is capable of
irritating other excretory organs, chief-
ly the skin and mucous membranes, with
damage to their epithelium. Externally
it acts as a severe irritant and caustic.

~~INTERNAL IRRITANTS~~ ,

~~CLASS D.~~ 2. NORMAL PRODUCTS IN EXCESS .

(that is, practically, substances usual in certain excretions but vicariously excreted).

URAEMIA .

This condition is caused by the accumulation within the system of substances that should be eliminated by the kidneys; these may be called for convenience "uraemic products."

These uraemic products are in reality composed of a number of poisons, That they act as irritants to various excretory outlets is shown by the accompanying vomiting and diarrhoea. Dr. Carter says that in uraemic vomiting there is a direct and free excretion of urinous

~~XX~~ *Fowler's Dictionary of Medicine . Article
"Uraemia", by William Carter, M.D.*

products by the gastric membrane. The peculiar odour of the skin of uraemic patients points to the excretion by the skin of some volatile abnormal substances. Moreover, urea has been found in the sweat and the breath of such patients. Landois and Stirling state;~~ST~~ "...In uraemic "conditions urea has been found crystal- "lised on the skin. When the secretion "of sweat is greatly increased, the "amount of the urea in the urine is "diminished, both in health and in "uraemia."

JAUNDICE

In this condition bile is sometimes excreted through the skin, as shown by the peculiar colour of the sweat. It is noteworthy that its early stage is often

^{XXI} *Physiology - Landois & Stirling . p. 352.*

Note. These authors also state that after a patient has taken arseniate of iron, arsenious acid has been found in the sweat, & iron in the urine. They also give as instances of pathological ~~Sweat~~; grape-sugar in Diabetes mellitus; uric acid & cystin very rarely; butyrate of lime in ague (sweating stage); & lactic acid in Puerperal fever.
(loc. cit.)

marked by irritation of the skin. In one instance that came under the writer's observation a woman complained of intense general prurigo, and a week later presented herself at hospital deeply jaundiced.

The most common excretory outlet of the bile in jaundice is by the kidney. In some cases it has appeared to the writer that ^{the bile} ~~it~~ may be to some extent excreted by the bowel, and thus give a yellowish colour to faeces that would otherwise be white. This method of excretion would certainly explain the intermittent faint colouring of the faeces that sometimes occurs in obstructive jaundice.

~~INTERNAL IRRITANTS, CLASS C.~~

3, Specific disease poisons (a) due to micro-organisms; (b) chemical poisons produced in body

(c) products of micro-organisms.

Due to micro-organisms -
(a). EXANTHEMS

Of these we shall consider two only with special relation to the skin eruption and to accompanying affections of other excretory organs.

MEASLES

Before the rash appears there is catarrh of conjunctiva and of mucous membrane of the nose, pharynx, and larynx. About the fourth day a papular rash appears on the face and soon involves the body and limbs. During the crisis the

Note A better classification of Class C, would be into -

rash may suddenly disappear, an occurrence which Kaposi says is always the result of a febrile complication. ~~The same~~ ^{XXII} observer states that the rash may now and then be altogether absent. In some cases the eruption may be multiform. Complications are affections of the lungs, air passages, eye and ear, or catarrh of the intestines; while renal affections are of rare occurrence.

In measles, then we have a specific poison that may inflict slight or severe damage on excretory epithelium. The inflammatory process may not affect the skin at all, or it may be suddenly shifted (disappearance of rash) from the skin to other organs.

^{XXII} Diseases of Skin. Kaposi. English Ed. 1895. p. 157.

SCARLATINA

The rash of scarlet fever begins as a punctate eruption on the upper part of chest about the second day of the fever. It rapidly becomes diffuse; lasts about three days; is followed by desquamation, a process which may extend over six weeks.

The rash may be multiform, and sometimes is altogether absent. The tongue and fauces are always inflamed. The intestinal duct may be affected, causing diarrhoea or croupous enteritis, the latter being sometimes accompanied with fatal haemorrhages. Albumen is present in the urine at an early stage in nearly all cases; indeed, renal disease, in the shape of catarrhal or glomerular nephritis coming on in the desquamative stage, is the most frequent complication.

There is a marked tendency to inflammation of serous and synovial membranes. At times the rash may suddenly and entirely disappear, an occurrence which usually points to serious disease of internal organs, such as lungs or brain.

Thus in scarlet fever we have a specific virus or its products which attacks all the excretory outlets, causing much damage to their epithelium. In the case of the skin we note that there may be no rash, ^{XXIII} and that the eruption may suddenly disappear; ^{XXIV} these facts point to absence of elimination of the virus (or its products) by the skin, or a sudden shifting of its channel of elimination to other organs.

^{XXIII} Kaposi speaks of scarlatina sine exanthemate with "complete absence of eruption & desquamation, while the angina & all the other symptoms of scarlatina may be present & may even be attended with fatal results." Kaposi, Dis. of Skin. English translation. 1895. p. 165.

^{XXIV} Kaposi. op. cit. p. 170.

~~CLASS C. SPECIFIC DISEASE POISONS~~

(7). Chemical; produced in system.

GOUT

This condition is due to some poison, presumably uric acid, ^{so far as we know} developed in the system. The injury it causes to excretory organs is best shown in those who inherit the gouty tendency and who suffer from what is known as "irregular gout." Persons affected in this way are liable to dyspepsia and various disorders of the alimentary canal; to skin troubles; to kidney mischief; and to inflammation of ~~various~~ mucous membranes.

^{xxv}
Crystals of urate of soda are found deposited in the tubules and interbular tissue of the kidneys; in the sputa of gouty bronchitis; and ^{as} ~~by~~ an efflorescence on the surface of the body in cases of

^{xxv}
Fowler's Dictionary of Medicine. Article
"Gout", by Dr. C. F. Shelly. 1890. p. 275.

gouty dermatitis. (Shelley)

The gouty poison, then, appears to affect all the excretory outlets, with severe damage, at any rate in chronic cases, to the epithelial structures.

RHEUMATISM

This condition is no doubt due to a specific poison circulating in the blood. The exact nature of the virus is not yet known, for the generally accepted view that it is a chemical poison, lactic acid, has been disputed by some modern authorities, such as Newsholme, who maintain it is a specific micro-organism. In either case it falls under the general

^{xxvi}
 Lettsomian Lectures. College of Physicians. London.
 1895. Arthur Newsholme M.D.

definition of an internal irritant.

The poison of rheumatism appears to be eliminated by the skin, if we may judge from its association with erythema, erythema nodosum, urticarial rashes, and with the remarkable purpuric manifestation known as peliosis rheumatica.

Besides these definite eruptions there can be no doubt that rheumatism is obscurely connected with a number of skin lesions. During the past few years the present writer has made a point of systematically inquiring into the history of patients under his care at a special hospital, and has found a large proportion of patients either directly or indirectly tainted with rheumatism.

The poison of rheumatism seemingly expends most of its violence upon the mesoblastic tissues, having a marked tendency to attack serous and synovial

membranes. Upon the ordinary excretory organs it appears to inflict only a moderate amount of damage. At times bronchitis, pneumonia and glycosuria develop during acute attacks.

~~CLASS C. SPECIFIC DISEASE POISONS~~

(C) Chemical products of micro organisms---~~Drugs~~

EXCRETION OF BACTERIAL PRODUCTS

It is still a moot point how far the rashes of the exanthems are to be ascribed to the influence of toxins and other products of micro-organisms, apart from the actual organisms themselves. In treatment by tuberculin, and by anti-toxin, however, there can be no such doubt, as the products of specific micro-organisms are in each case introduced directly into the system.

TUBERCULIN

It is a familiar observation that tuberculin, injected subcutaneously,

often gives rise to a transitory scarlatiniform rash. This fact was observed by the writer in a fair proportion of cases out of a large number treated by tuberculin in the year 1890 at the Birmingham Workhouse Infirmary. For the most part the fleeting eruptions in question were at first minutely punctate, but afterwards passed into a diffuse erythematous form.

ANTI-TOXIN

An eruption of the skin occurs in a large number of cases of diphtheria treated by the hypodermic injection of anti-toxin. Thus, an erythematous rash was reported by Drs. Washbourne, Goodall and Caird in 25 per cent of eighty cases. In 231 cases Dr. Moissard noted fourteen

^{xxvii} British Medical Journal. Dec. 23. 1894. p. 1418.

^{xxviii} Medical Press & Circular. Jan. 9. 1895. p. 34.

instances of urticaria, nine of polymorphic erythema, nine of scarlatiniform erythema, and one of purpura. In a collected series of 110 anti-toxin cases in private practice recently published in the British Medical Journal ^{XXIV} a skin complication is mentioned in 39. Dr. Tidswell, ^{XXV} Medical Officer of the New South Wales Board of Health out of 55 cases found 18 had rash. The Metropolitan Asylums Board ^{XXVI} report as follows:

"Among the undesirable effects of the
 "use of anti-toxin, by far the most
 "common was a rash, usually urticarial,
 "but sometimes erythematous or scarlatiniform. A rash was observed in 45.9
 "per cent of the cases treated with anti-toxin, and was often accompanied by fever,
 "which was observed in 29.6 per cent of
 "all the cases. In some it persisted

^{XXIX}

Diphtheria & the Anti-toxin treatment. Series of cases in private practice. Brit. Med. Journal. Jan. 18 to April 18, 1896.

^{XXX} Abstract of Dr. Tidswell's report. B.M.J. Feb. 1, 1896.

^{XXXI} Report of Metropolitan Asylums Board, Lond. 1896.

"for several days. Joint pains were
"observed in 4 per cent of the cases.
"They were rarely severe or accompanied
"by effusion and almost invariably passed
"off in a few days."

In both tuberculin and anti-toxin
we have bacterial products which some-
times inflame the skin when introduced
into the blood. At times they affect
both serous and synovial membranes.

GENERAL REMARKS ON THE INTERNAL IRRITANTS

In the foregoing summary a few types only have been chosen to illustrate each of the three divisions of internal irritants. They agree in the following cardinal points.

1. They are specific substances circulating in the blood.
2. They may set up a dermatitis.
3. They may cause inflammation of any of the other excretory organs, although their action is, as a rule, selective. In other words, internal irritants have the power of irritating any or all of the excretory organs.

These propositions are true of every kind of internal irritant. Some of the specific substances, such as arsenic and the virus of scarlatina, are highly in-

jurious to excretory epithelium, but it seems that all of them possess the same faculty to a greater or less extent. As a rule, each irritant affects its own peculiar channel of exit, but anomalies in this respect are common. Thus, there may be scarlet fever without rash, or long continued gout without kidney mischief.

The majority of drugs cause little or no irritation while being eliminated from the system. A typical instance of this class is sulphur, which is excreted by lungs, skin, bowel, and by various mucous membranes, so far as we know, without causing any damage.

In the irritant drugs the power of damaging epithelial structures is shown whether they gain access to the cells from without or within. For example,

arsenic, which externally is a powerful irritant and caustic to the skin, acts as a strong internal irritant to all the excretory organs. Cantharides, applied to the skin, causes a blister, and after absorption into the blood may set up inflammation and haemorrhage in its passage through the kidneys. On this point Dr. ^{xxxij} Murrell states that the majority of purgatives derived from the vegetable kingdom belong to the class of cutaneous irritants, and among them he cites croton oil, gamboge, and elaterium. Of these drugs, it is yet undecided whether any except ^{xxxij} elaterium is capable of purging after absorption through the skin. If that be the case then croton oil and gamboge must act as purgatives by virtue of their direct irritant action on the mucous membranes of the intestines. Castor oil, so far as the writer has been able

^{xxxij} "The Pharmacological Action of Purgatives,"
by Wm. Murrell. M.D. Med. Press & Circ.
Jan. 8. 1896.
^{xxxij} Stillé. Therapeutics. Vol. II. p. 459.

to ascertain, does not inflame the skin, but it sometimes acts as an aperient when rubbed into the skin of the abdomen, especially in children. The latter observation, as in the case of elaterium, appears to point to a power of selective excretion possessed by the bowels. Certainly mercury, whether administered by inunction, fumigation or hypodermic injection, may cause purgation which it would be difficult to explain on any other theory than that of direct excretory irritation of the bowel.

The foregoing facts suggest a wide excretory function for the ^{intestine} ~~bowel~~. It seems not impossible that the action of some purgatives, especially the delayed ones, may be accounted for by bowel excretion following absorption from the stomach. Moreover, this action of the

intestines as an excretory outlet may afford a key for results other than purgative. Morphia when injected subcutaneously has been detected in the ^{XXXIV} gastric juice and other secretions. In this way a dose of opium absorbed from the stomach might possibly be in part excreted through the intestine, with consequent disturbance of function.

In the case of specific disease poisons, just as with drugs, many pass off from the body and cause little mischief, as for instance the virus of chicken pox, mumps, vaccinia, rheumatism, or mild ptomaine poisonings. On the other hand, a certain number, like scarlatina, lead to severe and sometimes permanent damage of excretory organs. Lastly, no organ engaged ~~in~~ excretion is exempt from attack. In all these points

^{XXXIV}
*Dr. Berlin Klin. Wochens. 1889. XXVI. Dr. K. Horst,
 quoted by Wood (op. cit.)*

there is an exact analogy between the drugs and the specific disease poisons associated with skin lesions. Any individual member of either group may do little or much damage to organs during its elimination from the blood and all appear to be at times equally erratic in their choice of exits.

So far as drugs are concerned the theory of excretory irritation has been endorsed by Kaposi.^{xxxv} After speaking of reflex toxic phenomena he goes on;.....
 "In other cases the toxic substances,
 "being excreted through the cutaneous
 "capillaries, have a direct irritant and
 "paralytic action upon the peripheral
 "vessels and adjacent tissues, so that
 "the erythemata and the more intense in-
 "flammations (iodine and bromine acne)
 "develop only at those points." He also

xxxv

Diseases of Skin. by Kaposi. English Translation. 1895. p. 224.

quotes a similar opinion advanced by Behrend.

The proofs, direct and indirect, of the actual influence upon the skin of the internal irritants are chiefly:---

1. Some drugs, as iodine, bromine, arsenic, mercury, have been detected in the excretions of the inflamed skin as well as of other excretory organs.

2. Some non-irritant drugs, as sulphur, are excreted by the skin.

3. In gouty eczema urates have been found as an efflorescence on the skin surface, and urea in uraemic conditions.

4. In the case of some exanthems it seems probable that the specific micro-organisms themselves, apart from their products, are directly excreted by the skin, thus accounting for the infectiousness of affected individuals.

In the excretions of organs other than the skin the presence of the internal irritants, whether chemical or bacterial, has been often demonstrated by chemists and bacteriologists.

The cause of the rash in the exanthems is a subject that raises points of much interest as well as of practical importance. Hitherto, it has been usual to regard the desquamated skin of a scarlet fever patient as infectious. If so, the actual specific micro-organisms of the disease must have been excreted by the skin. Lately, however, there seems to be some doubt amongst sanitary experts as to the infectivity of a desquamating scarlet fever patient. Whatever the exact method of exit of the virus, it is clear that the living germs must in some way be eliminated from the

body. Scarlet fever would cease to exist did not the specific micro-organisms escape from the human body in a condition capable of spreading the disease. As this particular virus flourishes in the blood it follows that it must have been excreted in a living state by the skin or other excretory organs. The question is, through what particular channels of exit do the active germs escape. If through the kidney and bowel discharges then it is tolerably certain that effective measures are not taken in one case out of a hundred, even in our best ordered fever hospitals, to disinfect those evacuations. So too with the lungs, if the active germs are given off in the breath, what is done in the direction of aerial disinfection? Indeed, the only attempt at systematic disinfection of scarlet fever cases appears to be direct-

ed to the skin, and to clothing and other objects that have been in contact with the skin. Upon logical grounds there seems to be good reason for regarding with grave suspicion all excreta from a scarlet fever patient.

In typhoid fever the rash most commonly consists of small rose-coloured papules on the abdomen. At other times it appears on the general skin surface; thus, in a case under the writer's care the rash began on the legs and soon involved both upper and lower limbs. The reason of the almost constant localisation of the rash on the abdomen is not easy to conjecture. There may possibly be some venous or lymphatic channels by which either the organisms themselves or their products might reach the surface of the abdomen. At any rate, we know that typhoid bacilli are by no means con-

fined to the intestines, but are found
 in the abdominal cavity and in various
 parts of the body. ^{XXXVI} Dr. Grandmont, quoted
 by Stephenson, found them in the interior
 chamber of the eyeball, in a convalescent
 from the disease. He further introduced
 a pure culture of the organism into the
 vitreous humour of a rabbit, which, when
 killed three weeks later, was found to
 have numerous typhoid fever bacilli in
 the liver and intestines.

The direct excretion of pathogenic
 bacteria from the body has been definite-
 ly stated by Dr. Anton Weichselbaum ^{XXXVII} in the
 following passage....."Bacteria circulat-
 "ing in the blood may be excreted through
 "the kidneys, probably in cases where,
 "owing to some changes in the walls of
 "the vessels and membrana propria of the
 "urinary tubules, the passage of the
 "bacteria through them is rendered possible

^{XXXVI} *Archives d'Ophthalmologie*. 1892. p. 623.

^{XXXVII} *Elements of Pathological Histology*. Dr. Anton
 Weichselbaum; Translated W. R. Dawson, M.D.
 Lond. 1895. p. 116.

"or favoured. They may also, under
 "analogous conditions, traverse the
 "membrana propria of the mammary glands
 "and appear in the milk, or during
 "pregnancy may travel through the placenta
 ++ "into the foetus."

Prof. Unna, again, ^{xxxviii} speaks of certain
 infectious exanthems "due to a chemical,
 "locally active poison, produced by a
 "specific germ. Such are the roseola-
 "like spots in typhoid, typhus, dysentery,
 "diphtheria, pneumonia, recurrent fever,
 "acute rheumatism and influenza."
 These roseolae he regards as areas of
 reaction around more or less scattered
 emboli of the specific germ, upon which
 they are performing the office of
 "undertakers." From this passage it is
 clear that Unna has no doubt that many
 rashes are due to the presence of specific
 micro-organisms in the skin.

++ note. Dr. Weichselbaum does not state if in his
 opinion ~~the~~ changes in blood-vessels & membrana propria
 must precede the entry of micro-organisms into the system.
~~xxxviii~~ ^{viii}
 "Histopathology of Diseases of the Skin". By Dr. P. G. Unna,
 English Translation by Norman Walker, M.D.
 Edinburgh. 1896. p. 12.

Referring once more to de Grandmont's experiment, in which he injected a pure culture of the typhoid bacillus into the vitreous of a rabbit, and three weeks later found the specific bacilli in the intestine. If these organisms can be excreted by the bowel there is no reason, so far as one can see, why they should not be likewise eliminated by the skin and other excretory organs, seeing that the latter are all formed on a common anatomical and physiological basis. In addition to this logical possibility, however, we have direct evidence of the existence of active bacilli typhosi in the urine. Dr. Weichelsbaum ^{XXXIX} states definitely that the organisms of typhoid may be found in the urine sometimes even on the third day of the disease. At the same time it should be stated that, in common with most experimenters, he is

^{XXXIX}
Elements of Pathological Histology (cit.)
 p. 145.

opposed to de Grandmont's conclusion, which may be taken to assert the reproduction of enteric fever in the rabbit by injection of the specific bacillus into its tissues. "Typhoid fever," writes Weichelsbaum, ^{XI} "cannot be set up in animals" by inoculation with typhoid bacilli. "Injection of cultures into the blood or digestive tract may indeed kill rabbits, but this takes place, as it appears, not by infection but merely by intoxication."

The drift of modern opinion points to the conclusion that the rashes of specific fevers are for the most part connected with bacterial products rather than with the organisms themselves. This view is certainly supported by the frequent occurrence of eruptions during the hypodermic injection of tuberculin and ^{or} anti-toxin, which are both products of micro-organisms. The usual assumption

^{XI} Weichelsbaum. Op. Cit. loc. cit. p. 145.

appears to be that these particular rashes are the result of reflex nervous origin. The writer's suggestion is that they are the result of the excretion, or the attempted excretion, of an internal irritant by the skin. This explanation is borne out by the exactly analogous action of certain drugs and chemical irritants in the system. This theory of excretory irritation, be it noted, remains unaffected whether the rash of exanthems be traced ultimately to the influence of the organisms themselves or of their products.

ANTITOXIN RASH ---

In a paper read before the Dermatological Society of Great Britain and
XLI
 Ireland in 1895 the present writer suggested that the multiform rash commonly met with during the anti-toxin treatment of diphtheria might be due to excretory irritation. This view was supported by the analogy with tuberculin rash. The possibility of a nerve origin of this and other eruptions connected with internal irritants was discussed as follows.....

"In the case of scarlatina both the dermatitis and the nephritis are presumably due to a common cause. If the skin lesion be regarded as of nervous origin then a similar explanation should also apply to the kidney complication. However, I have never heard that anyone claimed a neuritic origin for either

XLI "A note on Antitoxin rash." David Walsh, M.B.
British Journal of Dermatology. Lond. Feb. 1895.
 P. 59.

"symptom in scarlatina. A similar line
 "of reasoning applies to the skin and
 "kidney inflammations following the in-
 "jection of anti-toxin. Both rash and
 "nephritis are traceable to a common cause,
 "and if the one be a neurosis, so probably
 "is the other. From my point of view,
 "the more likely explanation appears to
 "be that both are caused by direct
 "irritation of excretory epithelium."

This passage has been quoted in full
 because it deals with the chief altern-
 ative theory to excretory irritation in
 the class of skin inflammations under
 consideration. Dr. Radcliffe Crocker, ^{XLII}
 who admits the close relationship between
 gout and eczema, yet asserts that the
 skin conditions are "all instances of
 "irritation of the alimentary canal with
 "reflex capillary dilatation." This ex-
 planation, however, is not altogether

XLII

*Diseases of Skin. Radcliffe Crocker, M.D.
 2nd Ed. Lond. p. 123.*

satisfactory, as it omits to state how the uric acid reaches the intestine from the gouty tissues.

~~XLIII~~
Bouchard, in his work on Anti-intoxication makes the following statement which appears to bear on the theory of excretory irritation...."Je suppose que, "comme après l'ingestion de ces divers "médicaments, les vaso-moteurs cutanés "sont impressionés par l'action directe "du poison ou que leur perturbation est "le résultat d'un réflexe du système "nerveux. Pourtant, quand il s'agit de "sécrétions morbides comme l'acné, "l'eczéma, il est difficile d'admettre la "médiation du système nerveux. Ne vaut-il pas mieux incriminer l'élimination "d'acides gras volatils? Quelle que soit "d'ailleurs l'interprétation, le fait "empirique de l'enchainement entré la "dilatation de l'estomac et un grand

~~XLIII~~
"Auto-intoxications. par Ch. Bouchard, M.D.,
Paris. 187. p. 176.

"nombre de manifestations cutanées reste
 "certain, c'est bien un enchainement et
 "non une association fortuite. Comme
 "explication pathogénique, je vous propose
 "provisoirement l'intoxication."

CHLORAL RASH

The eruption due to the internal use of chloral may be mentioned here, as one of a class that can hardly be explained by the theory of excretory irritation.

There is an excellent figure in Mr. Hutchinson's ^{XLIV} Smaller Atlas showing both hands of a gentleman, aged 34, with dusky-red, erythematous patches, fairly symmetrical, lasting about three weeks. The patient experienced fifteen attacks,

^{XLIV} "Smaller Atlas of Clinical Surgery." Mr. Hutchinson. London. 1895. Plate V.

which were definitely connected with the taking of chloral. He was gouty, but otherwise in good health.

This eruption is probably connected with nervo-vascular disturbance. It does not follow, however, that the drug should not be able to cause direct excretory as well as reflex irritation. Indeed, we find that various scarlatini-form and bullous rashes have been traced to chloral. Arsenic behaves in a precisely similar way, for while we find it at one time causing a nervous lesion, like herpes zoster, at another it sets up various forms of local irritant skin eruptions.

It may be well to point out that the theory of excretory irritation as the cause of some forms of dermatitis would not be vitiated were it shown that certain other drug eruptions were of

nerve origin. The affirmative proposition is particular only and therefore would not be falsified by the production of a particular negative.

POLYMORPHISM OF DERMATITIS DUE TO INTERNAL IRRITANTS

Multiformity of lesion is the rule rather than the exception in the rashes connected with internal irritants. This variability of result does not strengthen the case for existing classifications, which are chiefly based on anatomical and morphological grounds. Indeed, it seems likely that in the near future the nomenclature of dermatology will be considerably altered.

As to the anatomical elements of the skin involved in the excretory

irritation, the process may begin in glands, papillae, or rete mucosa, in short, over as wide a field as that suggested by the multiform lesions. Anatomically, there is a striking resemblance between the ultimate structure of the skin and the kidney. Elsewhere the ^{XLV}writer has pointed out..."The Malpighian "tufts are very similar to the sweat "glands, while the renal tubules may be "compared with the palisade layer of "mucous cells overlying the papillae." This common structural plan is well described by Waller, ^{XLVI}who says of the kidney;... "As in all secreting or excreting glands, "the essential elements are a thin sheet "of blood separated by a membrane from a "layer of epithelial cells."

Once started, the dermatitis may go on to resolution, suppuration, abscess, gangrene, or may become chronic. Its

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- ^{XLV} "A note on Anti-toxin Rash," Brit. Journal Dermat. Feb. 1895. p. 61.
- ^{XLVI} "Human Physiology". A. Waller. Lond. 1895 p. 224.

survival may be due to the continued excretion of the original irritant, or to a secondary local development of microorganisms. If these explanations be true in the case of the skin, why should they not be true of other excretory organs? From the facts that have been advanced it seems clear that internal irritants, capable of inflaming the skin, may inflame any or all of the rest of the excretory organs. An acute inflammation is often the starting point of chronic disease in any given organ. If these premises be true, and if certain drugs be included among the internal irritants, as they are by our original definition, then it follows that certain drugs are often the starting point of chronic disease in excretory organs.

In other words, we arrive at the starting proposition that any single one

of the drugs we have placed among the internal irritants if introduced into the blood may set up chronic disease in any of the excretory organs. This possibility, therefore, applies to arsenic, mercury, cantharides, antimony, iodine, bromine, salicylic acid, and a great many other drugs commonly used in medicine. With regard to the point thus raised we may at once recall two facts, (1) the origin of an enormous amount of organic disease is absolutely unknown, and (2) modern pathology has taught us that in morbid processes the first step is the all important one. Again, we know that in gouty persons the long continued elimination of an irritant by the kidneys gives rise to chronic nephritis. Why should not the long continued excretion of arsenic, then, a drug which is intensely irritant to excretory epithelium,

++ Note. Against this suggested damage we have the experience, tolerably well confirmed, of the Arsenic eaters of Styria & Illyria, who live long lives.

also give rise to chronic nephritis? Yet arsenic is administered daily as a medicine, apparently with hardly a thought as to its possible ill effects upon internal organs. The same thing happens with many other irritant drugs used in medicine. It is clear that logically if the theory of excretory irritation be true then the use of any drug that inflames the skin should be carefully watched and safeguarded by careful regulation and intermission of dosage. For some years the writer has acted upon this deduction, arrived at upon purely theoretical grounds from the general law of excretory irritation.

There are many facts to illustrate the occasional disastrous effects of drugs used as curative agents. Instances are found in the severe iodine and bromine rashes, and in arsenical keratosis

and cancer. Another example has been described by Mr. Jonathan Hutchinson, ^{XLVII} who with characteristic acumen detected opacity of the vitreous humour in patients who had been taking long continued courses of arsenic.

Of late years there has been a reaction against the indiscriminate use of arsenic. Experience varies greatly as to its value in skin practice, and we are lost in wonder how so many good observers can arrive at totally different conclusions. From a consideration of the facts of erratic elimination it seems not unlikely that the arsenic is often excreted by the kidneys and does not reach the skin at all, just as the virus of scarlet fever now and then fails to produce a rash. Many other drugs have an equally uncertain and disappointing action in diseases of the skin, and, like arsenic, it

XLVII "On certain cases of Vitreous Opacity in connection with exceptional causes." By Jonathan Hutchinson. *Ophthalmic Review*. Vol III. No 87. Jan. 89.

The writer says :- "I have seen several cases in which, after a long use of arsenic for skin disease, permanent defects of vision, attended with muscae & opacities of the vitreous, ensued."

may be that they also are excreted by other organs. Anyway, it would seem rational to try and determine their action to the skin. This "drug determination" is a further deduction based on purely theoretical grounds from the general law of excretory irritation.

It is a common practice to prescribe a small dose of arsenic, say, three minims of Fowler's solution, to a patient suffering from a skin affection. There is no guarantee, however, that the drug does not pass away by the kidneys. Moreover, after a time the arsenic begins to accumulate in the system and is eliminated by various channels other than the kidney, yet it may still avoid the skin. The question arises, supposing arsenic to benefit the skin by its direct action, whether it would not be possible in the first place to determine its action to

the surface of the body by the use of a drug like pilocarpin. Some sort of natural determination probably takes place when the skin is previously irritated. It is a familiar observation that arsenic often acts adversely upon an acute eczema, and for that reason it is not recommended in active inflammatory conditions of the skin.

The reader has now had in review a mass of evidence to show that certain inflammations of the skin and of other excretory organs are the result of internal irritants circulating in the blood. There appears to be a further remarkable connection between the organic inflammations and those of serous and synovial membranes. In a sense the latter affections may be regarded as a sort of attempt at vicarious excretion.

In many cases specific pathogenic

organisms have been detected in the effusions of inflamed cavities. ^{XLVIII} Stephen-
son has quoted instances where the micro-organisms of enteric fever, of erysipelas, of tubercle, and of leprosy have been found in the anterior chamber of the eyeball associated with iritis. He quotes Mazza, who saw pleurisy, pericarditis, and poly-arthritis during an attack of gonorrhoea, and found the characteristic cocci in the pleuritic effusion. He also mentions Poncet, Clement Lucas, Fendick and others who detected gonococci in the joint effusions following purulent ophthalmia, a disease dependent on Neisser's gonococcus.

NERVE SYMPTOMS CAUSED BY INTERNAL IRRITANTS

Inquiry shows that nerve symptoms of a more or less severe nature are at times

^{XLVIII} "The excretory origin of certain forms of Trachoma & Cyclitis."
Sydney Stephenson. M.B. Lancet. Feb. 29. 1896.
Archives d'Ophthalmologie. 1881. Tome j. p. 213
Brit. Med. Journal. Feb. 28th, July 11th, Oct 10th. 1885.
Ibid. Oct. 31. 1885.

associated with all, or almost all, of the internal irritants. In this connection it should be remembered that both nerve cells and excretory cells are in close relation to their vascular supply, so that both are readily exposed to the action of blood-borne irritants. In either case the consequent irritation may be shown by (a) disturbance of function, (b) inflammatory changes of varying intensity.

Take the action of arsenic as a general internal irritant.

| ORGAN ----- | EFFECT ----- |
|----------------|---|
| Skin | Multiform dermatitis |
| Kidney | Nephritis |
| Stomach | Gastritis (when absorbed through skin) |
| Bowel | Enteritis, haemorrhages |
| Brain | Depression, vertigo convulsions, &c. |

Compare this with the effect of the scarlet fever poison on similar organs.

| ORGAN | EFFECT |
|---------|---------------------------------|
| ----- | ----- |
| Skin | Desquamative dermatitis |
| Kidney | Nephritis |
| Stomach | Gastritis |
| Bowel | Diarrhoea |
| Brain | Delirium, coma, convulsions. |

[The effects of alcohol, a powerful internal irritant, may be taken for further comparison.]

[Note The liver is acted upon more or less injuriously by nearly every member of the group of internal irritants. Indeed, its action as an excretory organ can hardly be appreciated without a full consideration of the bile in relation to varying blood conditions. In the present inquiry for the sake of simplicity it has

not been considered among the excretory organs. There can be no doubt, however, that if our conclusions be right as to excretory irritation in general, they will apply to the liver in particular.

SUMMARY AND CONCLUSIONS

Taking the skin as one of a group of excreting organs we find it suffers from various forms of inflammation in the presence of a number of specific substances circulating in the blood, to which we have given the name of "internal irritants." In some cases the relationship between the excretions of the skin and an underlying pathological condition is evident to our senses. Thus we can sometimes see urates on the skin surface and bile in the sweat. In

other instances we detect by means of chemical and biological tests the presence of an internal irritant in the matters given off by the skin. Besides which, we have daily before our eyes the objective rash that gives unerring evidence of a specific irritant within the body. But these symptomatic skin eruptions are so constantly associated not only with internal irritants but also with inflammations of other excretory organs that it seems impossible to avoid the conclusion that the whole series of these phenomena are due to a common cause. The origin of the general process we take to be the disturbance set up by the eliminatory passage of the internal irritant through the essential cells of the excretory organs.

Note. Because we cannot find.

CONCLUSIONS

The main conclusions arrived at in the course of this inquiry may be summed up as follows.

1. That some forms of dermatitis are due to the irritation set up by the excretion from the blood of certain specific substances, (here called "internal irritants.")

2. That the skin suffers as one of a group of excretory organs; and that all those organs may be similarly affected by the internal irritants.

3. That the internal irritants sometimes inflame the serous and synovial membranes.

4. That proof is afforded, by means of chemical and biological tests, of the frequent passage of some of the internal irritants from the blood into

the excretions, and into serous and synovial effusions.

5. That the internal irritants often effect the nerve centres.

6. That any internal irritant which inflames the skin may be suspected of inflaming other excretory outlets.

7. That any drug which inflames the skin should be administered with great caution, owing to the possibility of damage to other organs.

8. That it may be possible at times to guide the action of a remedy to the organ it is wished to affect.

9. That, conversely, any particular organ may be relieved of the stress of elimination.

10. That the law of excretory irritation has a wide application to general pathology.

Postscriptum .

The attempt to present the theory of excretory irritation within the ordinary limits of a graduation thesis has led to a considerable condensation of arguments & of literary treatment .For the sake of brevity no mention has been made of alcohol , which may be regarded as an internal irritant with a most damaging effect on all excretory outlets . The desquamating lesion , again , in Savill's disease , epidemic dermatitis , has the appearance of resulting from the cutaneous excretion of an intensely irritating product or virus of unknown origin .Another of many omissions has been the amyloid degeneration of organs associated with chronic suppuration , a condition also possibly of excretory origin . However , the reader who has grasped the principle of the theory will find little difficulty in recognising the width & importance of its further applications .

Inflammation has been claimed as the broad basis of modern pathology , but if the law of excretory irritation be true we must go a step further back to the starting point of a large class of inflammations in the disturbed metabolism of the excretory cell .

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